Supporting Information

for

Strategic Design of 2,2'-Bipyridine Derivatives to Modulate Metal–Amyloid-β Aggregation

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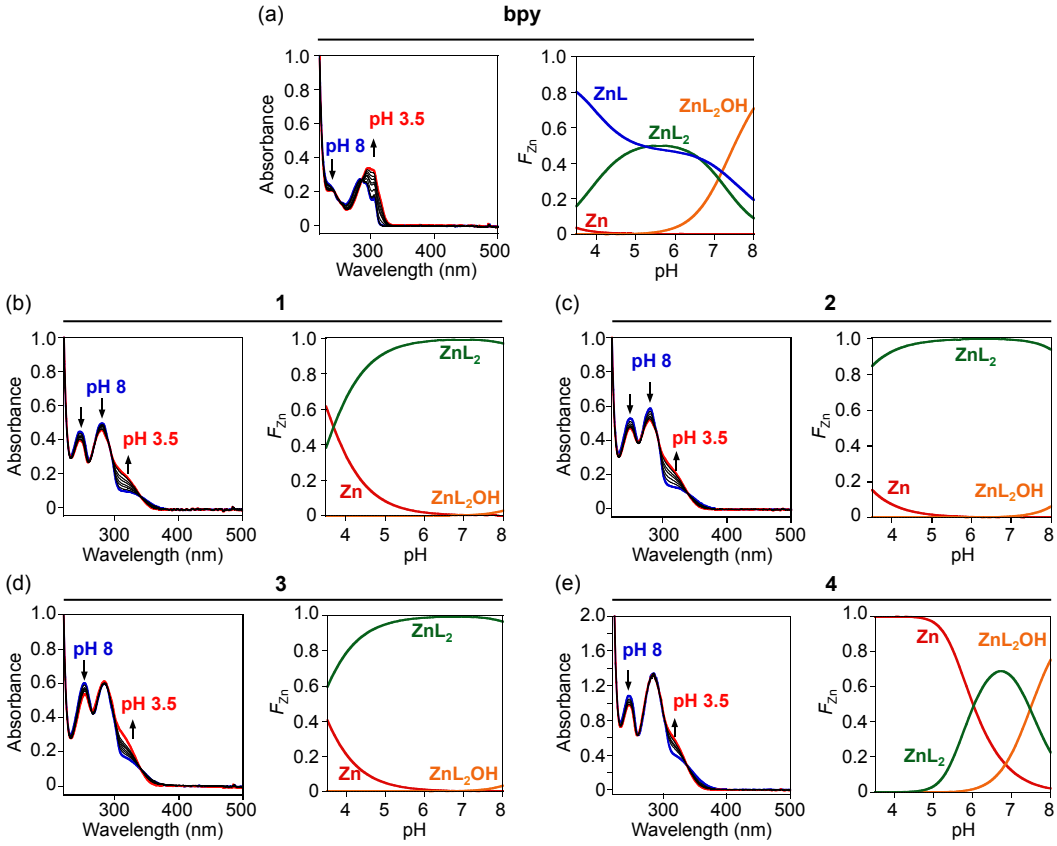

				logβ^a		
		L =	**bpy**	**1**	**2**	**3**	**4**
Zn + 2L + OH	⇌	$Zn(L)_2(OH)$	5.45(4)	9.83(9)	12.57(9)	11.02(0)	6.43(9)
Zn + 2L	⇌	$Zn(L)_2$	12.56(0)	19.37(4)	21.76(0)	20.49(1)	13.91(5)
Zn + L	⇌	Zn(L)	7.29(6)	—	—	—	—
pZn (= -log[$Zn_{unchelated}$]; pH 6.6 / 7.4)			7.30 / 7.31	7.05 / 7.55	7.77 / 8.27	7.30 / 7.80	4.96 / 5.50

Figure S1. Solution speciation studies of Zn(II)–L complexes (L = **bpy** and **1**–**4**). UV–vis variable-pH titration spectra (left) and solution speciation diagrams (right) of (a) **bpy**, (b) **1**, (c) **2**, (d) **3**, and (e) **4** upon incubation with Zn(II) (F_{Zn} = fraction of species at given pH). Stability constants (logβ) of Zn(II)–L complexes are summarized in the table (bottom). Charges are omitted for clarity. Conditions: [L] = 25 μM (for **bpy** and **1**–**3**) or 100 μM (for **4**); [$ZnCl_2$] = 12.5 μM (for **bpy** and **1**–**3**) or 50 μM (for **4**); room temperature. [a]The error in the last digit is shown in the parentheses.

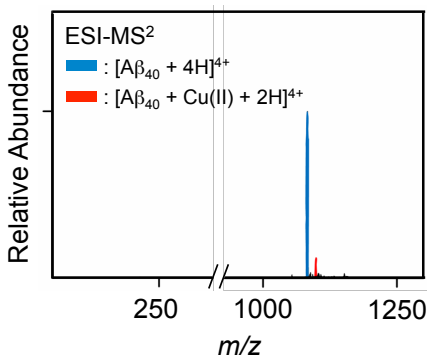

Figure S2. Tandem MS (ESI-MS^2) spectrum of the +4-charged peak at 1151 *m/z* from the sample containing $A\beta_{40}$, Cu(II), and **4**. The ESI-MS^2 results supported that the peak was assigned to $[A\beta + 2Cu + 2K + 4H_2O - 2H]^{4+}$, thus indicating no formation of a ternary complex composed of $A\beta_{40}$, Cu(II), and **4**. Conditions: $[A\beta_{40}]$ = 100 μM; $[CuCl_2]$ = 100 μM; [compound] = 500 μM; 20 mM ammonium acetate, pH 7.2 (1% v/v DMSO); 37 °C; 1 h incubation; no agitation; 10-fold diluted samples were injected to the mass spectrometer. The relative abundance of each spectrum was individually normalized based on the highest peak.

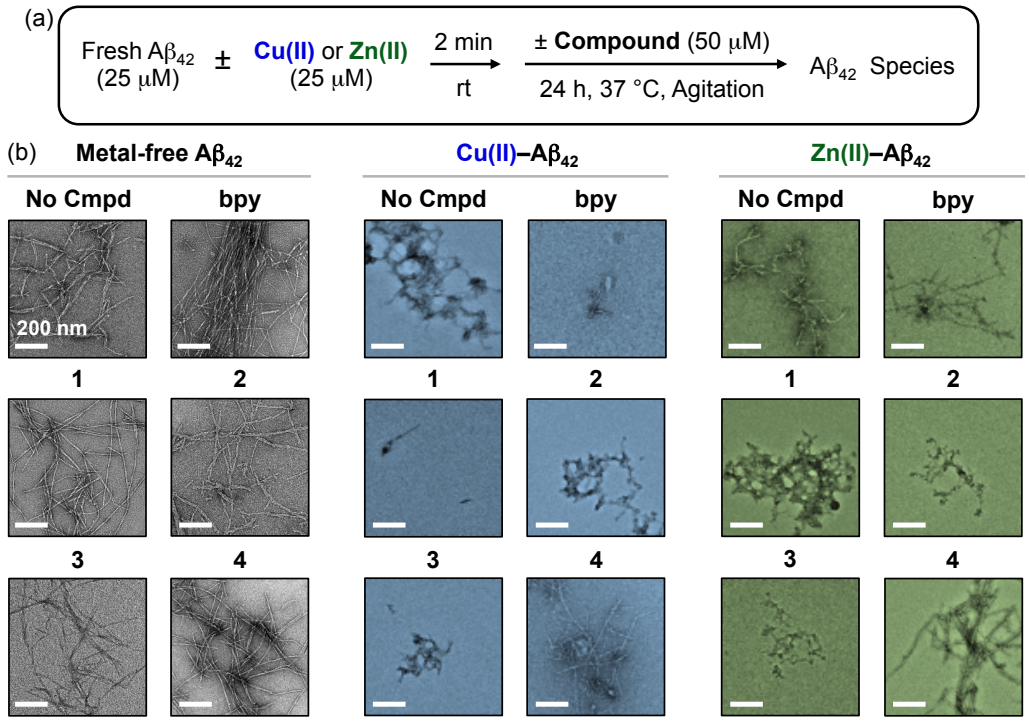

Figure S3. TEM images of the resultant metal-free $A\beta_{42}$ and metal–$A\beta_{42}$ aggregates generated upon treatment with **bpy** and **1**–**4**. (a) Scheme of the experiments. (b) TEM images of the 24 h incubated $A\beta_{42}$ samples from Figure 6. Scale bar = 200 nm.

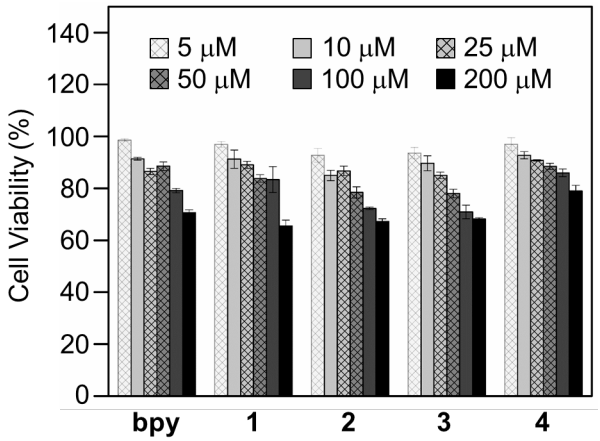

Figure S4. Toxicity of **bpy** and **1**–**4** in SH-SY5Y cells. Cells were treated with **bpy** or **1**–**4** for 24 h at 37 °C. Cell viability (%) was determined by the MTT assay. The viability values were calculated compared to those of cells treated with DMSO only (1% v/v). Error bars represent the standard error from three independent experiments ($P < 0.05$).

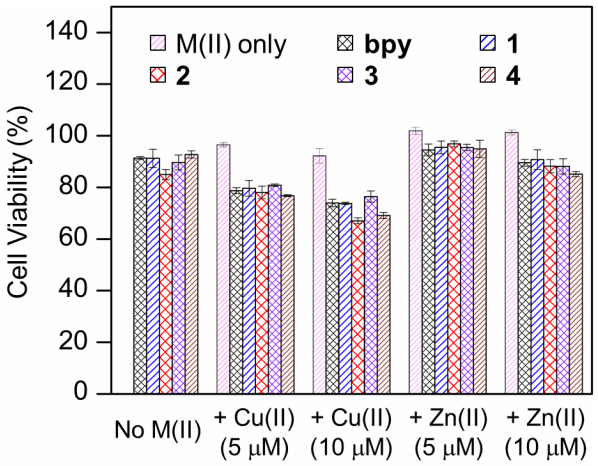

Figure S5. Toxicity of **bpy** and **1**–**4** in SH-SY5Y cells in the presence of metal ions. Cells were treated with **bpy** or **1**–**4** (10 μM) with metal ions (5 or 10 μM) for 24 h at 37 °C. Cell viability (%) was determined by the MTT assay. The viability values of cells were calculated compared to those of cells treated with DMSO only (1% v/v). Error bars represent the standard deviation from three independent experiments ($P < 0.05$).